A CASE OF HYDROPHOBIA:

WITH

REMARKS ON THE PATHOLOGICAL PHYSIOLOGY OF THE DISEASE.

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[Reprinted from The Boston Medical and Surgical Journal, November 1, 1878.]

CAMBRIDGE:
Printed at the Riverside Press.
1878.

A CASE OF HYDROPHOBIA:

WITH REMARKS ON THE PATHOLOGICAL PHYSIOLOGY OF THE DISEASE.[1]

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Case. (Reported by Mr. J. B. Wheeler, house-pupil at the Massachusetts General Hospital.) A. B., of Boston, age sixty-eight, lamplighter, had of late years enjoyed very good health, with the exception of an epithelioma of the lower lip, which was "drawn" by a female cancer-doctor three weeks before entrance. He was a large, powerful man, in remarkably good muscular condition for his time of life. Mentally, he seemed a fine specimen of an uneducated American. He was ignorant but intelligent, of a manly character, and much respected in his neighborhood. On July 19th — about seven weeks before his admission to the hospital — he was bitten in the right thumb by a strange cat which he attempted to caress. The wound was not cauterized. A "bone-felon" ensued, which was treated with various poultices, and necrosis of the distal phalanx of the thumb occurred.

On the morning of September 9th the patient appeared at the Massachusetts General Hospital, and was given a bed in the wards of Dr. C. B. Porter, whose place was then being temporarily filled by Dr. T. B. Curtis. He complained of difficulty of swallowing, first noticed at supper the evening before, no such trouble having been experienced at dinner, and of entire inability to eat his breakfast that morning. This outbreak of characteristic symptoms had not been preceded by any change of character or emotional disturbance. During the night, however, he had been very restless, and at breakfast he found that the attempt to put liquid in his mouth brought on a paroxysm characterized by choking, gasping, and by rapid, irregular movements of the arms and legs. Dr. C. C. Street, who was called in, refrained from acquainting the patient with the nature or gravity of his symptoms, but advised him to enter the hospital at once.

At the time of his arrival the patient appeared very "nervous," excited, and restless, though perfectly rational. He could not remain seated, but in the course of a few minutes, while conversing, would

[1] Read before the Boston Society for Medical Observation, October 21, 1878.

walk about the room, throw himself on the bed, and then suddenly jump up and sit in a chair. His expression was anxious, although he did not seem troubled about himself, and complained only of the paroxysms, which came on with every attempt at swallowing. He talked rapidly, but with frequent hesitations in the middle of his sentences, as if out of breath, — a circumstance which his wife said she had never noticed before. His mouth was dry, and some viscid saliva stuck to his lips and teeth. The pulse was 88.

A private room was assigned to the patient. He made little or no complaint, and was disposed to converse in a rational and sociable way, but he was very restless, roaming about almost incessantly in quest of fresh air. At six P. M. one sixth of a grain of sulphate of morphia was given subcutaneously, with no apparent effect. At eleven P. M. one fifth was given, and at 2.30 A. M. of the next day one third of a grain. The only effect was to make the patient overstate the length of the short naps which he took. In the morning he reported himself as having passed a very comfortable night and slept several hours, the truth being that he walked the corridors and piazza almost all night, and did not sleep in all over half an hour. At 2.30 A. M. he asked if his paroxysms could be due to the bite of the cat, "for," he said, "a cat hates to get wet, and wetting me always brings on the trouble."

September 10th, ten A. M. The patient is a little more comfortable this morning, and appears less nervous and excited. He had slept from nine to 9.30 A. M.

At eleven o'clock a consultation was held, at which Drs. Cabot, Shaw, Warren, and Curtis were present. A glass of water was offered to the patient, which he refused to take, saying that he could not stand so much as that, but he would take it from a teaspoon. On taking up the water in the spoon he evinced some discomfort and agitation, but continued to raise the spoon. As it came within a foot of his lips he began to gasp violently, his features worked, and his hand shook. He finally almost tossed the water into his mouth, losing the greater part of it, and staggered about the room, gasping and groaning. The respiration seemed at this moment wholly costal, and was performed with great effort, the elbows being jerked upwards with every inspiration. The paroxysm lasted about half a minute.

The act of swallowing did not appear to distress him, for he could go through the motions of deglutition without any trouble. The approach of liquid to his mouth, however, would at once cause distress. The same effects were occasioned by wetting the face, by dipping the tip of one finger into a cup of water, by trying to hold a lump of ice in the hand, or by a sudden and strong current of air. On being gently fanned as he sat talking, the patient sprang instantly from his chair, with a look of surprise and alarm, and went into a violent paroxysm similar

to those produced by attempts to drink. He described his sensations as resembling those which would result if a pailful of ice-water were suddenly thrown in one's face. Nevertheless, a slight draught, he said, was agreeable, but if it came too strong it took his breath away in a very unpleasant manner. He complained continually of want of air and of oppression, and was all the time moving restlessly about, going into the corridors and on to the piazza, in quest of more air.

The patient did not appear to entertain the slightest suspicion of his being affected with hydrophobia, of which disease he was apparently wholly ignorant; nor did he, at first, seem to connect his sufferings in any way with the injury to his thumb caused by the cat bite. He talked a good deal about his cancer (which was in a state of progressing ulceration), and was enthusiastic and garrulous on the subject of the cure which he supposed had been effected. In order to divert his attention from the graver disorder, the cancer was always spoken of, in his presence, as if it were the interesting feature of his case, and the patient remained to the end in ignorance of the nature of his disease.

At the consultation which was held no doubt was entertained of the existence of hydrophobia. It was decided that the treatment by curare[1] should be instituted, and that the administration of the drug should be persevered in, with rapidly increasing doses, until relief of the paroxysms or the production of commencing toxic symptoms (muscular paresis). It was also decided that, the rectum having first been emptied by an opening enema, frequent nutritive enemata should be injected. The order was consequently given to the attendants to administer every four hours an enema of four ounces, warm water, beef tea, and wine whey being used in turn.

At 2.10 P. M. the first subcutaneous injection of curare, containing one third grain, was given by Dr. G. B. Shattuck, who kindly took charge of the patient for a couple of hours. The drug was procured from Theodore Metcalf & Co., and was imported by them from E. Merck, of Darmstadt. It was in the form of dark brown, hard, dry, glistening fragments, like fine gravel. The solution, containing one part of curare in ten, was prepared in the hospital shortly before being administered.

At 2.20 P. M. respiration superficial, 20 to a minute. At 2.30, a copious opening enema of soap, salt, molasses, and warm water was administered, and operated freely in five minutes. At three, four ounces of wine whey were given per rectum. At 3.15, the pulse was 80, the respiration 22. Face a little flushed. No other change was observed.

At 3.20 P. M., curare one third of a grain. At five, an enema of beef tea (four ounces). At 5.15, curare one third of a grain. Pulse and res-

[1] For the arguments in favor of this plan of medication see the Boston Medical and Surgical Journal, March 7, 1878, page 315, and August 29th, page 264.

piration as before. At six, curare one half grain. No change. At seven, enema of warm water (four ounces). At 8.45, curare three fourths of a grain. No effect was thus far visible, except slight flushing of the face. At nine, curare three fourths of a grain. At 10.45, curare three fourths of a grain.

At eleven P. M. the patient was much more restless; so much so that a night-watcher was found necessary. He complained of shortness of breath, with occasional paroxysms such as have been already described. A slight paroxysm was occasioned by the administration of the last enema. Pulse 90; respiration varying from 40 to 60.

September 11th, 2.45 A. M. Pulse 90; respiration 25 to 30. Curare three fourths of a grain. At one A. M. enema of water (four ounces), by which a slight paroxysm was excited. Patient expressed a suspicion that there was some connection between his present sufferings and the cat-bite. At three A. M. very restless. Curare, a grain. Enema of wine whey, four ounces.

At 3.30 A. M. the patient appeared very weak, and staggered when walking from one side of the corridor to the other. His knees seemed to give way under him. He had hitherto walked with a firm, but somewhat rolling gait, not remarkable in one who had formerly been a seafaring man. Mind clear.

At five A. M. enema of beef tea. Curare, a grain. As the stock of curare in the hospital had given out, a one per cent. solution, kindly furnished by Dr. A. N. Blodgett and previously tested by him, was used. The patient was restless, insisting on going home, and complaining that the curare was making him so weak that he would not be able to walk home. He did not, however, appear particularly weak at this time. As the administration of the last enema had excited a violent paroxysm, and as the attacks were recurring quite frequently, the enemata were discontinued. About this time, early in the morning of the 11th, the patient began to spit large quantities of very thick, tenacious saliva. The act of exspuition was accompanied by violent efforts to throw the spittle as far as possible. At each act of spitting the head was jerked back as the spittle left the mouth, and the lips were drawn away from the teeth, the object of this manœuvre being, apparently, to avoid the contact of the saliva as much as possible.

At 6.15 A. M. the patient, who in the course of the preceding eighteen hours had received six and a half grains of curare, escaped from his watcher, the latter having probably fallen asleep. He ran out of the ward and across the hospital grounds, clambered with great agility and *apparently unimpaired muscular force* (according to the account given by those who saw him) over the high fence, and got into Charles Street. He was soon found in a yard opposite the jail, and was brought back to the hospital without making much resistance. After his return

the paroxysms succeeded each other at intervals of from five to ten minutes. Pain in the head was complained of as being constantly present and becoming excruciating during the paroxysms. His attendants were frequently called upon to hold his head and compress his forehead, which proceeding seemed to afford some relief. As the patient felt the approach of a paroxysm he would suddenly spring to his feet from his bed or chair and throw himself on his knees before some article of furniture, against which he would lean, while spitting frantically in the way already described, and screaming, "For God's sake, hold my head, or it will burst!" During the paroxysms, and sometimes between them, he would struggle violently, at times trying to rush out of the room, or to throw himself out of the window. Three men were required to hold him. He made no attempts to bite or scratch, but struck with his fists three or four times. Occasionally he would berate and curse the attendants, insisting that they were imprisoning him, and giving him curare to make him drunk. One of the ward-tenders, whose appearance reminded him of his grandson, was the only person who remained on good terms with him. This attendant he insisted on having near him, and would occasionally caress him and joke with him. At times, his utterances were delirious. He frequently inquired with anxiety whether the sink in his kitchen had been cleaned out last night. His remarks were often jocular, and sometimes somewhat obscene. He perspired freely the whole time.

At seven A. M., curare one grain (Dr. Blodgett's solution). The patient tried to swallow a wineglassful of water, but failed to get more than a teaspoonful into his mouth. At eight A. M. he succeeded in swallowing a wineglassful of cold water; a paroxysm ensued.

At 8.15, curare one and a half grains (Dr. Blodgett's solution). Behavior somewhat less violent; paroxysms less frequent, and rather less severe. Pulse strong and hard, from 96 to 120. At nine A. M. the patient's wife arrived. Her presence seemed to soothe him a little. When he felt a paroxysm approaching he would send his wife out of the room, and let her return when it was over. At the height of the paroxysms he would exclaim that he was going to die, that he could not stand it any longer; but in the intervals he frequently expressed confident hopes of recovery.

At 10.15, curare one and a half grains (hospital ten per cent. solution). Paroxysms about the same. General behavior less violent. At eleven, suffered more than before, if possible. Curare two grains. At 11.30, showed failure of strength. Pulse feeble. Shirt and flannel changed because soaked with perspiration. At twelve, was somewhat easier. Was quite playful and affectionate with his favorite attendant, whose beard he pulled, then laughed, and tried to kiss him.

At one P. M., much weaker. Reclined on the floor, with head rest-

ing against a chair. *Paroxysms every two minutes.* No longer asked to have his head held, but wished to be supported so that he could spit more easily. Curare two grains.[1] At 1.20, pulse very weak. His movements appeared feeble, but the paroxysms continued unchanged. At 1.30, pulse imperceptible, breathing rapid, pupils normal, paroxysms still as frequent as before, but each one weaker than the preceding one. About this time he was lifted upon the bed, and while there became excited, and tried to get up and leave the room, displaying *considerable muscular strength* in his struggles. After this he very rapidly grew weaker, lost consciousness, and died quietly, without any paroxysmal phenomena. The paroxysms continued until within a few minutes of death, but were very feeble, and somewhat less frequent than they had been a few hours before.

The autopsy was made by Dr. E. G. Cutler. The brain and spinal cord were placed in hardening fluids and reserved for microscopical examination.

Remarks. — The striking resemblance of a hydrophobic paroxysm to the shock of a shower-bath — a resemblance recognized both by the patient and by his attendants — will, I think, give us the key to the pathological physiology of the disease now under consideration. Let us, then, first investigate, so far as our existing knowledge allows, the analogous dyspnœic phenomena observable under certain circumstances in healthy persons, with a view to ascertaining the nature and mode of production of these manifestations. For this purpose a few facts of experimental physiology relating to the functions of the respiratory centre must be recalled.

Respiration is effected by the alternate contraction and relaxation of certain muscles animated by motor impulses proceeding from the respiratory centre in the medulla oblongata. This nervous centre is constantly at work, supplying the needful amount of motor stimulus to the respiratory muscles. In order that the activity of the respiratory movements may to a certain extent be accommodated to the varying needs of the organism, an arrangement exists by which the activity of the respiratory centre, when excessive, or for the time being superfluous or harmful, can be diminished or even wholly annulled. This result is

[1] These last doses of curare were, to say the least, superfluous. I do not believe that I should have allowed them to be given if I had been able at that time to be present. I was, however, engaged in operating upon a case of strangulated hernia, and could not then give my attention, as I should have wished, to the hydrophobic patient. The last doses were administered, in accordance with the instructions given at the outset, for the reason that the paroxysms were growing more and more frequent, and that the patient's struggles were still at times very vigorous. In fact, with the exception, perhaps, of the profuse perspiration, no unequivocal signs of curare-poisoning, not attributable to the progress of the disease itself, were observed. I am, however, persuaded that it must be very difficult, if not impossible, to discriminate between the toxic effects of the drug and the natural symptoms of the disease in its advanced stage. My reasons for this opinion will be given later. — T. B. C.

accomplished by the operation of what is called an *inhibitory* influence. Inhibition, or "arrest," consists in a paralyzing or stilling effect exerted by a centripetal, sensory impression upon an active nervous centre supplying motor stimulus. Inhibitory action is therefore just the opposite of reflex phenomena, though not without analogy to them, for, in the case of a reflex function, an excito-motor influence is exerted, whereas the effect produced by inhibition, on the contrary, is depresso-motor. The well-known experiment of Goltz, in which a frog's heart is suddenly stopped by a tap upon the abdomen, is one of the most familiar examples of inhibition.

Of all the inhibitory influences to which the respiratory centre is subjected, none is more typical of inhibition in general, or more striking in the directness, completeness, and simplicity of its action, than that exerted by the *superior laryngeal* branch of the vagus. Rosenthal's experiments, confirmed by Claude Bernard and many others, and also borne out by the recent researches of Burkart,[1] show that when the central end of this nerve is stimulated, after its denudation and division, respiration is immediately suspended, the diaphragm, paralyzed and relaxed, being thrown into an attitude of extreme expiration.[2] According to Brown-Séquard, the same result can be produced by direct irritation of certain parts of the medulla. Respiration ceases, the heart continuing to beat for a while more or less rapidly and strongly. "This arrest of respiration," he says, "is *not due to a reflex spasm* of the diaphragm or of the intercostal muscles, but to a cessation of action of these muscles, caused without doubt by the cessation of action of the respiratory centre."[3]

A similar influence — ranging in the intensity of its effects from the production of a more or less marked condition of breathlessness, dyspnœa, gasping, or respiratory distress and anxiety to sudden death by paralytic apnœa — is exerted by a variety of peripheral stimuli. Thus Schiff has shown that powerful excitations of the nerves of general sensation, particularly of the fifth pair, cause slowing of the respiratory movements. It is not only the nerves of sensation, conscious or unconscious, which can thus convey an inhibitory influence to the respiratory centre. A similar effect is produced by psychical impressions (exciting or depressing emotions) proceeding from the emotional regions of the brain to the medulla. This fact is exemplified by the breathlessness which is experienced under circumstances of great alarm or excitement, as well as by the depressed state of the respiratory function caused by profound grief. In the latter case arrears of breathing have to be made up by frequent semi-volitional sighs.

[1] Pflüger's Archiv, vol. xvi., page 427. Revue des Sciences médicales, vol. xii., page 424.

[2] According to Arloing and Tripier (Archives de Physiologie, etc., vol. iv., 1871, page 735) the left vagus is chiefly concerned in controlling the respiratory centre, while the activity of the heart is principally under the influence of the right vagus.

[3] Archives de Physiologie, etc., 1869, page 767.

As in the case of bodily pain, this physiological function of respiratory inhibition, though familiar to us chiefly by its unpleasant or harmful manifestations, really subserves a useful end in providing a means of protection for the respiratory organs against injurious external agencies. The superior laryngeal nerve, whose inhibitory influence is so remarkable, supplies sensation to the mucous membrane of the base of the tongue, of the upper part of the anterior wall of the œsophagus, of the epiglottis, and, lastly, to the laryngeal mucous membrane. When it is stimulated by an irritating contact, such as attends the penetration of foreign bodies, liquids, or irritating vapors and gases into the air passages, paralysis of the diaphragm at once takes place, with *extreme expiratory relaxation*, so that inspiration is rendered for the time being impossible. The further penetration of the irritating agent is thus prevented.

This same protecting agency is brought into play in every normal act of deglutition to prevent the entrance of solid or liquid food through the glottis. "The first requisite for the act of swallowing," says Professor Dalton,[1] "is the suspension of respiration. This takes place at the beginning of deglutition by a nervous mechanism which it is difficult to describe, but which may be designated as an 'action of arrest.' The same nervous impression which excites by reflex action the constrictors of the pharynx suspends for a time the movements of inspiration. This effect is very perceptible in the ordinary act of swallowing, and was witnessed by Waller and Prévost in many of their experiments on this subject; galvanization of the central extremity of the superior laryngeal nerve causing immediate relaxation of the diaphragm, with stoppage of its movements."

Swallowing is not the only physiological act normally attended by respiratory inhibition. The act of inspiration itself, according to Wundt, is a constantly recurring cause of the same phenomenon. When the lungs are fully inflated an inhibitory impression is conveyed through certain fibres of the vagus to the respiratory centre. Inspiration is thus rendered, as it were, self-inhibiting.

Without dwelling further on our experimental knowledge of this function of the nervous system, I will briefly recall a few familiar illustrations of its effects as witnessed and experienced in human beings. In the first place, all persons know the uncomfortable sensations caused by a shower-bath, consisting in breathlessness and respiratory distress, often attended by great anxiety or even terror, and most marked in children, and in timid, emotional, so-called "nervous" persons, in whom there is reason to believe that the emotional regions of the hemispheres are but imperfectly under the control of the higher (volitional

[1] Physiology, sixth edition, 1875, page 367.

and rational) cerebral functions. The same distressing state of apnœa is not unfrequently caused in sea-bathers by wading into the sea, and some persons find themselves wholly unable to withstand the deterrent effect so produced. Water splashed in the face and on the chest has a similar action, as also submerging the face in a basin of water. A glass of strong, hot, steaming punch will sometimes "take one's breath away" by the same mechanism.

Sudden death by apnœa, caused in the same way as the transient disturbances mentioned above, occasionally takes place. Such, for instance, is the mechanism of sudden death in tracheotomy, in fractures and other violent injuries of the larynx, and in garroting.[1] The mysterious drowning of expert swimmers, who suddenly sink, with or without a cry of distress, — an accident commonly attributed to a supposed "cramp," — may, perhaps, also be due to respiratory inhibition with expiratory relaxation of the diaphragm, resulting from the penetration of water into the larynx. The immediate sinking of the swimmer would thus be accounted for. Of all the examples of sudden death due to this agency, however, none is more interesting than the fatal accident which occasionally takes places in the first stage of chloroformization.[2] In such cases respiration suddenly ceases, the heart continuing for a short while to beat,[3] as in Brown-Séquard's experiments alluded to above. According to this view, the so-called "chloroformic idiosyncrasy," invented to account for certain inexplicable deaths caused by the inhalation of chloroform, consists simply in an exceptional susceptibility to respiratory inhibition, originating, perhaps, in emotional or traumatic collapse. Herein lies the great superiority of ether over chloroform. In consequence of its pungent odor, ether undoubtedly occasions a certain degree of initial respiratory distress, lasting until the mucous membranes exposed to its vapor have become locally anæsthetized. Its local action, however, is far less irritating than that of chloroform, and it has never, I believe, been known to cause sudden death in the first stage of administration, in the unexpected way peculiar to chloroform.

The last illustration of respiratory inhibition in disease which I shall adduce is perhaps somewhat hypothetical. The opinion has been advanced that paralysis of the diaphragm might be one of the causes of

[1] Leven has shown, by experiments on animals, that a ligature tied around the trachea, so as to constrict it somewhat, without preventing the passage of air, causes immediate slowing of the respiration, and that a ligature tied tightly around the trachea causes instant death. If, however, the vagi are previously cut the ligature no longer causes sudden death, but kills more slowly by asphyxic accumulation of carbonic acid. Archives de Physiologie, etc., 1870, page 176.

[2] Mathieu and Urbain attribute certain deaths by chloroform to the arrest of respiration, caused by irritation of the laryngeal mucous membrane. Archives de Physiologie, etc., vol. iv., page 586.

[3] Giraldès. Nouveau Dictionnaire de Médecine, etc., article Anesthésie, vol. ii., page 46.

asthmatic attacks.[1] However this may be, one would certainly expect that so important a function as respiratory inhibition would, like all the other physiological functions, be liable to morbid derangements. It seems, therefore, rather surprising that its disturbances should have played so small a part in pathology.

Having thus passed in review some of the phenomena of respiratory inhibition in health and disease, we will now carefully consider the manifestations observable in cases of hydrophobia.

The disease is chiefly characterized by certain paroxysms commonly alluded to as "convulsions" or "spasms," and erroneously supposed to bear a more or less close resemblance to the spasms of tetanus. The first symptom to attract particular attention, in most cases, is an inability to swallow. The difficulty at first ensues upon attempts to drink cold water, but before long the patient finds it impossible to swallow warm fluids, solids, or even his saliva. At the same time there is not necessarily any difficulty in executing the movements of deglutition. Our patient was very positive that he could do so, and demonstrated the fact by going through the motions of swallowing before his attendants. The inability to drink is due to the fact that the access of liquids or solids to the fauces at once excites a violent and distressing paroxysm of apnœa. Of all the various occasional causes to which the paroxysms are due, this is the one which operates earliest and most powerfully. There is no dread of water, but a dread of apnœa, — an extreme apprehension of the agonizing paroxysms found by experience to recur on every renewed attempt to drink.

The paroxysms — presenting the same features, however originated — result from a variety of occasional causes, which it will be sufficient to enumerate as follows: (1.) Attempts to drink (hydrophobia) or to swallow food or saliva. (2.) Penetration of saliva into the fauces, whence the ceaseless spitting, deglutition being impossible. (3.) Currents of air, caused by draughts, wind, and fanning (aerophobia). (4.) Cold or wet applications to the surface of the lips, face, extremities, or body. (5.) Other peripheral irritations, such as the administration of an enema. (6.) Luminous appearances and glistening objects, including water, mirrors, lights, etc. (7.) Sounds, as of doors opening, of people walking and talking. (8.) Mental impressions, giving rise to

[1] Bamberger, quoted by J. B. Berkart, on Asthma, London, 1878, page 37.

Professor Sée asserts that "the dyspnœa of asthmatic patients is due, in the immense majority of cases, to a centripetal excitation of the vagus and of the superior laryngeal nerve." (Nouveau Dictionnaire de Médecine, article Asthme, vol. iii., page 630.)

Dr. B. Edson recently reported a case of severe dyspnœa under the title of Paralysis of the Diaphragm. (New York Medical Record, September 21, 1878, page 229.) The opinion was subsequently expressed that Dr. Edson's case might have been hay fever of a somewhat exceptional character. (W. C. Wey, New York Medical Record, October 12, 1878, page 289; G. M. Beard, New York Medical Record, November 2, 1878, page 348.)

alarming or depressing emotions (pantophobia). (9.) Attempts to draw a full breath.[1]

Noting, as we pass, the similarity of these provoking agencies to those concerned in the causation of the normal phenomena of respiratory inhibition in healthy subjects, let us now consider the characteristic features of the hydrophobic paroxysms with a view to determining, if possible, their nature and the mechanism of their production.

The paroxysms, when existing in their least marked degree, — as when excited in the outset of a case by some trifling cause, such as carrying a spoonful of water to the lips, or dipping the tip of a finger into a cup of water, — consist in sudden attacks of breathlessness, marked by a rapid succession of quick, shallow, sobbing gasps, during which the inspiratory efforts are of the "costo-superior type." At the same time the patient shudders, and anxiety is depicted on his countenance. The phenomena constituting such a paroxysm have a most striking resemblance, as has often been observed,[2] to what takes place in a timid, "nervous" person under a cold shower-bath. The resemblance is by no means merely a superficial one. We shall soon find that there is good reason to believe that the phenomena are identical in kind, if not in degree, in the two cases.

When more violent, the attacks — whether caused by attempts to swallow, by fanning, or occurring spontaneously, under the influence of an excitation to be explained presently — take place as follows: the patient, having been for a while in comparative quiet and comfort, resting from his sufferings, suddenly starts violently from his bed, calling perhaps for help, and struggles up on to his feet, with an expression of distress, alarm, or terror on his face. In his efforts to get quickly into a suitable posture on the floor, and to free himself from surrounding trammels, the muscular exertion of body and limbs is at times violen and frantic.

[1] Jaccoud, rehearsing the causes of the paroxysms, says: "The respiratory movements themselves may be the exciting agency. Youatt observed this fact in rabid dogs, and Bright recognized it in a patient who, on this account, was careful to avoid making full inspirations." (Pathologie Interne, 1877, vol. ii., page 931.)

See also Romberg, Lehrbuch der Nervenkrankheiten, Berlin, 1840.

[2] In a case observed by Dr. S. Cabot at the Massachusetts General Hospital in 1854, the paroxysms were described as follows: "They more resemble the catching of the breath which one experiences in taking a shower-bath, though more violent." (Massachusetts General Hospital Surgical Records, vol. lx., page 88.)

Romberg also notes the resemblance. (Loco citato, page 510.)

Jaccoud (loco citato, page 931) describes "a sudden arrest of respiration, quite analogous to that which one experiences on plunging into an ice-cold bath, or on receiving a cold shower-bath." Nevertheless, he considers that the paroxysms are spasmodic or hyperkinetic manifestations, and states that "a condition of excessive reflex tension in the foci of the nerves presiding over respiration and deglutition is the essential characteristic feature of rabies in man." His theory, thus enunciated, is exactly the reverse of that advocated in this paper. The two theories differ as completely as a reflex, or excito-motor, differs from an inhibitory, or depresso-motor, phenomenon.

See also Bohinger, Ziemssen's Cyclopædia, American translation, vol. iii., page 491.

Then, in the case of a spontaneous paroxysm, while gasping and struggling for breath, behaving, in short, very much like a drowning man who feels himself going under, the patient, having got himself into a kneeling or crouching posture, sets to work *spitting* in a peculiar way, as described in our reported case. Such an attack lasts perhaps half a minute, after which, having cleared his mouth and fauces of the tenacious spittle, the patient sinks back exhausted, to rest until his next seizure.

These spontaneous paroxysms, recurring with a certain degree of regularity, more or less frequently, seem to be caused by the gradual accumulation of the saliva, which the patient cannot swallow nor yet get rid of without great and fatiguing exertion, on account of its viscid character. When the saliva is sufficiently abundant to trickle into the pharynx, or in any way to be noticed by the patient, a paroxysm is suddenly originated. At first this result is probably due to the mechanical irritation of the fauces; but, later, the mental apprehension aroused by the prospect of an impending paroxysm seems to be the chief disturbing agency. The patient soon learns to associate his sufferings with their determining conditions, and, in consequence of his anticipation of the expected result, a paroxysm is begotten by the fear of a paroxysm.

In the phenomena observed in this case, as also in two other cases which I have seen, there was, properly speaking, *no evidence of spasm or convulsions*,[1] — unless a drowning man, unable to swim and thrashing about in the water, or a man clutched by the throat and struggling frantically for life, can be said to have convulsions. Great muscular exertion there is certainly, but it is of a somewhat rational and volitional kind. At the same time the breathing is short, quick, labored, thoracic, and conspicuously of the costo-superior type, the supplementary and volitional inspiratory forces being brought vigorously into play.[2]

[1] Dr. S. Cabot, who in the course of his extensive experience has seen some seven or eight cases of hydrophobia, testifies unhesitatingly to the entire absence of true spasms and convulsions in all of them.

[2] In paralysis of the diaphragm, as described by Duchenne, "the respiratory movements are usually more frequent than in health; the respiration does not, however, appear to be much embarrassed so long as the patient keeps still. . . . . But if he makes any exertion to walk or to talk, if he undergoes any excitement, his respiration quickens; the trapezius, sterno-mastoid, serrati, pectoralis major, and latissimus dorsi muscles contract; the face reddens; the patient is breathless; he is obliged, if walking, to sit down; if talking, he must keep taking breath to finish his sentence," etc. (Electrisation localisée, 1872, page 908.)

Parrot (Archives de Physiologie, etc., 1871, page 240) is of the opinion that an unfailing sign of impending death (agony) is to be found in certain symptoms which, he says, are indicative of paralysis of the diaphragm. These are, in the first place, an inspiratory sinking in of the epigastrium and hypochondria, and, in the second place, pronounced *costo superior inspiratory efforts*. These last, which he says are observed in all cases of diaphragmatic paralysis, were plainly visible during the paroxysms in the case of my patient. I regret having omitted to observe the respiratory movements of the abdomen in this case, as I might thereby perhaps have been able to verify the correctness of my theory of the parox-

The appearances all suggest the idea of violent efforts to supplement the sudden failure of respiration, together with a frantic struggle to get free from some suffocating agency.

The patient's sensations were described by himself as follows: —

Q. Why cannot you drink? *A.* Because it takes my breath away.[1]

Q. Why do you start so when you are fanned? *A.* Because I cannot bear the wind.

Q. What does it feel like? *A.* As it would if you had a pailful of cold water thrown in your face.

In the intervals between the paroxysms, there are evidences of important disturbances, both physical and mental. The patient sighs frequently, and at times catches his breath with a sort of gasp or sob; he complains of suffering constantly from various distressing sensations, such as a feeling of præcordial oppression, of breathlessness, and of respiratory anxiety, together with a constant craving for more air.

The psychical symptoms — sometimes preceding the advent of the paroxysms (*stadium melancholicum*), and always more or less marked during the acme of the disease — consist in emotional disturbances (depression and excitement), with impairment of the restraining powers exerted by the higher cerebral functions of reason and volition. These disturbances take the forms of mental depression, anxiety, fear, suspicion of attendants, together with great restlessness and excitability, culminating in a state of delirium or even of mania. Marked sexual excitement (satyriasis, nymphomania) has occasionally been observed.[2] In the case of a female whom I saw at the Hotel Dieu in 1869, when interne under Voillemier, nymphomania was present in a most remarkable and scandalous degree, ceasing only with life.

Finally, rapidly progressing general exhaustion occurs, due largely to privation of food and drink and to the almost complete lack of sleep, accompanied by ceaseless muscular exertion. Death takes place either quietly, from gradual cessation of respiration, or during a final paroxysm.

Having passed in review the determining causes of the hydrophobic paroxysms and the appearances which they present, I will now venture to express an opinion as to their nature. Judging, then, by the strong resemblance which they bear to familiar phenomena of respiratory inhibition, as regards both their provoking causes and their characteristic features, subjective as well as objective, I believe the paroxysms to consist in sudden attacks of *paralytic apnœa*, due to temporary, partial or

ysm, by ascertaining whether the violent inspiratory efforts of the patient were accompanied by the epigastric depression described by Parrot. Some other observer will perhaps repair this omission.

[1] See Dr. Sansom's case, Lancet, September 7, 1878, page 329: "There seemed to be a 'stop' in his breath when he tried to drink."

[2] See Jaccoud, loco citato, page 932.

complete, inhibition of the respiratory centre, taking place under the influence of peripheric impressions. The inhibitory stimulus proceeds first from the area of distribution of the superior laryngeal nerve, being originated by attempts to drink and by accumulated saliva; secondly, from the area of the fifth pair, as a result of wetting the lips or face, and of fanning; thirdly, from the nerves of sensation of the trunk and limbs; fourthly, from the nerves of special sense; and, fifthly, from the emotional regions of the hemispheres, a paroxysm being excited by the fear of a paroxysm.

According to this view, the most characteristic phenomena of hydrophobia, the paroxysms, consist simply in greatly exaggerated manifestations of a familiar physiological function, namely, the function of respiratory "arrest" or inhibition, experimentally studied by Rosenthal, Brown-Séquard, Claude Bernard, Burkart, and others.

With regard to the origin or mode of production of the paroxysms of respiratory inhibition two suppositions can be made: either the inhibitory stimuli are increased, or they meet with less power of resistance in the respiratory centre. Let us for a moment consider these two views.

Increased inhibitory stimuli would be due to a sort of hyperæsthesia [1] of all the parts of the peripheral nervous system from which centripetal inhibitory impressions are known to proceed. With the exception, however, of the paroxysms themselves, whose production we are trying to account for, no evidence can be adduced to show that any such condition of hyperæsthesia capable of intensifying the inhibitory impressions exists.

Diminished resistance of the respiratory centre to occasional inhibitory influences seems a much more plausible explanation of the paroxysms. Such a condition of impaired resistance would readily result from the marked diminution of respiratory activity, existing permanently in hydrophobic patients. According to this view the positive stimulation supplied by the respiratory centre being constantly inadequate, occasional negative (inhibitory) stimuli produce exaggerated effects, and therefore *seem intensified.*

This functionally depressed condition of the respiratory centre, entailing diminished powers of resistance to inhibitory influences, is doubtless due, primarily and principally, to the structural changes taking place in the respiratory centre itself.[2] The impairment of function, resulting from such local alterations, is probably intensified by an addi-

[1] Jaccoud attributes the production of paroxysms, under the influence of fanning, the contact of liquids, etc., to a "cutaneous hyperæsthesia" (loco citato, page 931). Bollinger (Ziemssen's Cyclopædia, American translation, vol. iii., page 486) says that "this excessive *hyperæsthesia* is manifestly the cause of the aerophobia," etc.

[2] Dr. W. R. Gowers, having made microscopic examinations of the brain and cord in four cases of hydrophobia, says: "The region in which the lesions were most intense corre-

tional depressing influence, proceeding from the morbidly active emotional regions of the hemispheres to the medulla.

The following scheme, then, seems in a tolerably satisfactory manner to coördinate and account for the phenomena of hydrophobia: —

The activity of the respiratory centre — being kept in a permanent state of depression, "below par," so to speak, in consequence of local alterations of structure, and also in consequence of depressing influences proceeding from the diseased emotional regions of the brain — is thereby rendered liable at any moment to become reduced to zero (paroxysm of paralytic apnœa) by slight inhibitory stimuli of peripheral origin; death eventually resulting, during or after a final paroxysm, from entire failure of the inspiratory forces.

The *therapeutical deductions* suggested by this theory of hydrophobia are, I regret to say, chiefly negative, taking the form of counterindications.

The methods of treatment hitherto advocated have generally been based upon the unwarranted but undisputed assumption that the disease was of a convulsive nature, the paroxysms themselves being looked upon as the expressions of an exalted condition of the excito-motor functions of the medulla and spinal cord. To combat the supposed "spasms," all the amyosthenic and depresso-motor agents have successively been tried, curare being the drug for which the most enthusiastic and most recent claims of efficacy have been raised.[1] If, however, the theory now advocated is accepted, if the disease is characterized by *deficient* excito-motor activity, and if the paroxysms, instead of being spasmodic, are in reality paralytic manifestations, then all depresso-motor medications must be looked upon as distinctly counterindicated. Curare, in particular, which exerts an almost exclusively amyosthenic action, — by virtue of its power to prevent motor stimuli from reaching the muscular fibres, — would seem to be the very last drug to be recommended, since it kills by producing paralysis of the diaphragm. Full doses of curare would have the effect of rendering the patient powerless to struggle; in this way the outward manifestations of his sufferings would be more or less repressed. The tendency to paralytic apnœa, however, could only be intensified, and the fatal termination would thereby be hastened.

In the case of my patient, notwithstanding theoretical objections to the medication, and doubts as to the authenticity of the cases[2] of hydro-

sponds to that in which experimental physiology has located the "respiratory centre of the medulla." (Pathological Transactions, 1877.)

The results of Dr. Gowers' investigations have been confirmed by Dr. R. H. Fitz. (Boston Medical and Surgical Journal, August 29, 1878.)

[1] For a statement of the theory upon which the treatment of hydrophobia by curare is based, see Offenburg's case in the Medical Times and Gazette, October 6, 1877, page 396.

[2] In Dr. Watson's case (American Journal of the Medical Sciences, July, 1876) it is not

phobia reported to have been so cured, it was decided, in deference to the favorable evidence [1] lately adduced, to try the treatment by curare. In so desperate a disease any treatment which seems to hold out the slightest promise of efficacy should be given a fair trial. The result in this case, however, was as unsatisfactory as possible. Several other cases are, moreover, on record, in which the same treatment proved unavailing.[2] Such being the case, I believe that, unless more convincing reasons for its use are brought forward, curare should be abandoned in the treatment of hydrophobia.[3]

Until some means of treatment shall have been discovered by which the progress of the pathogenetic processes of hydrophobia can be arrested, the resources of therapeutics must be limited to the treatment of the symptoms of the disease. The objects to be aimed at are the relief of the patient's sufferings, the prevention or mitigation of the paroxysms, the administration of food and drink, and, finally, as easy and painless a death as may be procured without the fatal termination being actually hastened by our therapeutical measures.

The frequency and intensity of the paroxysms might be diminished in two ways, namely, by preventing the reception or the transmission of peripheral inhibitory stimuli, or by increasing the activity of the respiratory centre, so as to diminish the liability to total failure under slight inhibitory influences.

With a view to suppressing the peripheral inhibitory impressions narcotics and anæsthetics have been largely tried.

Chloroformic anæsthesia, if it could be established and maintained, would perhaps cause the paroxysms to be more or less suspended. This result would, however, be difficult if not impossible to obtain. Chloroform inhalation, as we have seen, occasionally kills apparently healthy subjects by respiratory inhibition, in consequence of its irritating action upon the laryngeal mucous membrane, and would therefore be unlikely

only the recovery of the patient after three small doses of curare, amounting in all to about one third of a grain, which makes one distrust the diagnosis. The report of the case shows that the patient was throughout able to swallow liquids and solids in abundance, and that he was not apparently affected by bathing his hands and face in water.

[1] Boston Medical and Surgical Journal, March 7, 1878, page 315; also Medical Times and Gazette, October 6, 1877, page 396, and December 1, 1877.

[2] Boston Medical and Surgical Journal, March 7, 1878, page 315.

[3] Only on one supposition could curare be expected to have any but an unfavorable effect in hydrophobia. If the paralyzing influence which this drug exerts upon the cardiac inhibitory fibres of the vagus is shared by the respiratory inhibitory fibres, and if this favorable effect is not wholly overbalanced by the harmful amyosthenic action of the drug, then curare might be of service by shutting off, to a certain extent, one of the chief sources of inhibitory impressions. The liability to the production of paroxysms might thus be somewhat diminished. According to Paul Bert, however, the vagi preserve their inhibitory power over the cardiac function in curarized mammifera, impairment of the inhibitory function of the vagi having been observed only in frogs.

to be well tolerated in hydrophobia.[1] Moreover, when chloroformic anæsthesia is fully established, a very depressing influence is exerted upon the respiratory and cardiac centres.

Ether is liable to somewhat the same objections, though in a very much less marked degree, and probably offers the nearest approach to a means of euthanasia, without exasperation of the most dangerous symptoms, and without undue risk of precipitating the probably inevitable fatal termination by paralytic apnœa.

Chloral hydrate administered by enema or by intravenous injection, although possessing no curative virtue, seems to have been of service in some cases by inducing sleep, and by diminishing somewhat the frequency and violence of the paroxysms.[2] Such a result of its narcotic properties must of course be highly welcome, provided that the drug, while mitigating the sufferings of the patient, — and thereby masking the progress of the disease, — does not at the same time impair his enfeebled powers, and hasten the fatal termination. Vulpian,[3] having lately investigated the action of anæsthetics (chloroform, ether, and chloral) upon the respiratory centre, found that in chloralized dogs a very small additional dose of the drug was apt to produce death by apnœa, the respiratory centre being paralyzed. He also found that in dogs anæsthetized by chloral the respiratory movements, when arrested by irritation of the central end of the cut vagi, do not spontaneously become reëstablished, as they promptly do in animals not under the influence of an anæsthetic. His experiments show that the narcotic action of chloral is extended to the respiratory centre, and that under its influence the inhibitory arrest of breathing is apt to be irreparable. These considerations, applicable to all the narcotic medications when pushed to the full production of anæsthesia, should be taken carefully into account in any attempt to determine the usefulness of drugs in hydrophobia.

Such seems to be the limited extent to which narcotics and anæsthetics may be expected to be of benefit. If, on the other hand, it were possible to increase the activity of the respiratory centre, which is in a

[1] In Sansom's case (Lancet, September 7, 1878, page 329) "it was determined that the ulnar nerve should be divided, and the scar on the hand removed; and further, that the administration of chloroform should be attempted. Immediately on its application, however, the patient ceased breathing, and turned to a cadaverous tint, with a feeble, fluttering, intermittent pulse. . . . Artificial respiration did no good. After about a minute a few gasping respirations occurred. Afterwards breathing was more regular, though interrupted with much gasping." In his concluding remarks Dr. Sansom says: "Though chloral was highly beneficial, it was as distinctly proved that the inhalation of chloroform was dangerous."

[2] See Sansom, loco citato; also Prévost and Hanot, Gazette hebdomadaire, 1876, page 364.

[3] Comptes rendus de l'Académie des Sciences, May 27, 1878; Revue des Sciences médicales, vol. xii., page 487.

condition of such marked depression in hydrophobia, the tendency to paroxysmal respiratory inhibition would probably be counteracted. Belladonna or atropia, in moderate doses, is known to act as a respiratory stimulant, whence, perhaps, its usefulness in some forms of asthma (Trousseau), and in opium poisoning, where death by paralytic apnœa is impending. It has been asserted that atropia has the property of paralyzing the laryngeal fibres of the vagus which inhibit respiration, but Keuschel seems to have shown that such is not the case, so that the increased respiratory activity caused by this drug is now attributed to its direct stimulating action upon the respiratory centre.[1] When very large doses are given this centre is paralyzed. These considerations would lead us to expect some slight benefit in hydrophobia from small or moderate doses of atropia.

Opium, in small or moderate doses, activates the respiratory function, thus exerting a property which is often utilized in the treatment of disease.[2] In large or toxic doses, on the contrary, it has a depressing effect upon the respiratory centre, and kills by producing paralytic apnœa. In hydrophobia, as was observed by Magendie and others, very large doses of the drug seem to be tolerated, but whether their effect as regards the respiratory function is favorable or the reverse is difficult to determine. In the treatment of hydrophobia I think caution should be exercised in the use of all drugs which have a tendency to produce depression of the respiratory centre, and, for this reason, opium should be given, I think, only in moderate doses, such as are known to have a eupnœic effect.

In conclusion of these remarks, which are intended to be only suggestive, and have no pretension to an exhaustive character, I would call attention to an important point deserving consideration in connection with the administration of powerful drugs in large doses to hydrophobic patients. In all diseased conditions in which the secretion of urine is defective, accumulation of drugs within the system is apt to occur, in consequence of the fact that their elimination is prevented or interfered with. This is known to be not unfrequently the case in Bright's disease.[3] In hydrophobia, where a condition approximating anuria exists, it seems not unlikely that drugs may produce cumulative effects to an unexpectedly injurious extent. This consideration should, I think, be borne in mind, especially in connection with the use of agents whose *toxic* effects are likely to be unfavorable.

[1] Von Boeck, Ziemssen's Cyclopædia, American translation, vol. xvii., page 675.

[2] Huchard, in a paper on the use of opium in heart disease, calls attention to the excellent effects of morphia, administered subcutaneously, in all forms of dyspnœa, especially in such as occur in paroxysms, as in asthma, and in those forms which are due to a nervous disturbance. (Journal de Thérapeutique, Nos. 1 and 2, 1877.)

[3] See Chauvet on the danger of powerful drugs in renal disease, Paris, 1877.